

Literature

Concerning the New Remedy

For Tuberculosis.

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Pasteur; nor is there any doubt as to the claims of Professor Koch to the discovery of the tubercle bacillus.

In the month of March, 1882, Dr. Koch announced to the medical world that he had discovered the existence of a microbe hitherto unknown, and to which was given the name of the tubercle bacillus. He described how he had subjected diseased organs of numbers of men and animals to microscopic examination, and found, in all cases, the tubercles infested with a minute, rod-shaped parasite, which, by means of a special staining process, he differentiated from the surrounding tissue. He says: "It was in the highest degree impressive to observe in the center of the tubercle cell the minute organism which had created it."

Professor Klein differs from this view. He says: "I cannot agree with Koch, Watson Cheyne, and others, who maintain that each tubercle owes its origin to the immigration of the bacilli, for there is no difficulty in ascertaining that, in human tuberculosis, in tuberculosis of cattle, and in artificially induced tuberculosis of guinea-pigs and rabbits, there are met with tubercles in various stages, young and old, in which no trace of a bacillus is to be found, whereas in the same section caseous tubercle may be present containing numbers of tubercle bacilli."

Transferring directly by inoculation the tuberculous matter from diseased animals to healthy ones he in every instance reproduced the disease. To meet the objection that it was not the parasite itself, but some virus in which it was embedded, he cultivated his bacilli artificially for long periods of time and through many successive generations.

This was confirmed by reliable investigations, and thus was established the existence of the tubercle bacillus and its discovery by him, and up to this time everything is plain sailing.

From the date of this announcement (1882) by Professor Koch up till October, 1889, nothing particularly new was heard on the subject, and as far as the literature on the tubercle bacillus goes, we have every reason to believe that the search for a toxic agent to combat the disease of tuberculosis and the ravages of the tubercle bacillus has been fruitless. Indeed, to all outside appearances, the tubercle bacillus, having been once discovered, was to

be left unmolested to pursue its ravages on helpless humanity. But in reality it was being followed up by tireless and relentless foes.

On October 19th, 1889, was published in the *Medical News*, of Philadelphia, by Dr. Samuel G. Dixon, at that time Professor of Hygiene to the University of Pennsylvania, a monograph announcing his discovery of the hitherto-unknown forms of the tubercle bacillus.

In the previous summer, whilst investigating different methods of technique and manipulation abroad, Dr. Dixon was led to believe that the bacillus could be cultivated so as to show lower forms of virulent life; and following this idea up by a series of experiments, he was in a short time able to produce the hitherto-unnoticed forms of the bacilli, some club-shaped, others curved, and others again branched.

From the growths thus obtained he proceeded to make a series of tube inoculations, from which he grew bacilli corresponding in every respect to the ordinary rod-shaped tubercle bacillus.

Having obtained these results, he propounded two hypotheses: 1st, That by a thorough filtering out of bacilli from tuberculous material a filtrate might be obtained and attenuated, so that by systematic inoculations a change might be produced in living animal tissues that would enable them to resist virulent tubercle bacilli. 2d, To bring about a chemical change or physical change in living tissues that would resist tubercular phthisis, it is possible that inoculation with the bacillus would have to be made; yet, before this could be done, the power of the virulent bacilli would have to be diminished, otherwise the result would be most disastrous. He added further that he had reduced the tubercle bacillus to a condition that, when inoculated into the animal economy, caused a resistance to the disease.

To use a military metaphor, this was the first note proclaiming that an active campaign had been opened on the tubercle bacillus, and specifying in terms as definite as possible the means by which the war was carried into the enemy's country.

The announcement of this discovery was widely circulated and commented upon, and reprints of the article were forwarded to

Drs. Von Pettenkofer, Koch, Louder-Brunton, and other scientific investigators.

The International Medical Congress was appointed to meet in Berlin in August, 1890, and more than usual interest attached to its meeting, as it was generally rumored that some important papers on the subject of the tubercle bacillus would be read on that occasion.

Nor was this rumor falsified, and the interest of the meeting may be said to have culminated as Professor Koch rose to address the assembled physicians, and when he stated that he had hit upon a substance which had the power of preventing the growth of the tubercle bacillus, it was greeted with loud applause. It was then stated that the bacillus of tuberculosis in man and chickens was very similar, and he inferred that the latter is a special species of the organic matter supposed to lie at the root of pulmonary consumption. He also announced that the direct action of solar light on the tubercle bacillus destroys in a certain length of time, varying from a few minutes to several hours, the virulence of this microbe.

It will be convenient to quote verbatim from that portion of the paper proclaiming his discovery of a toxic agent: "In spite of this failure—to effect any result on tuberculous animals with chemical substances—I have not allowed myself to be discouraged from prosecuting the search for growth-hindering remedies, and I have at last hit upon a substance which has the power of preventing the growth of tubercle bacilli, not only in a test tube, but in the body of an animal. All experiments in tuberculosis are, as every one who has had experience of them has sufficiently discovered, of very long duration. My researches on this substance, therefore, although they have already occupied me for nearly a year, are not yet completed, and I can only say this much about them, that guinea-pigs, which, as is well known, are extraordinarily susceptible to tuberculosis, if exposed to the influence of this substance, cease to react to the inoculation of tuberculous virus, and that in guinea-pigs suffering from general tuberculosis, even to a high degree, the morbid process can be brought completely to a standstill without the body being in any way inju-

riously affected. From these researches I in the meantime do not draw any further conclusions than that the possibility of rendering pathogenic bacteria in the living body harmless without injury to the latter, which has hitherto been justly doubted, has been thereby established." (Address before the Medical Congress in Berlin, August, 1890.)

It will be observed that Professor Koch in his paper makes two points: 1st, The action of solar light and a high degree of heat in destroying the virulence of the microbe; 2d, The fact that he had produced a substance the effect of which was to prevent the growth of the tubercle bacilli in the body of an animal, and that he produced a condition in that animal that was immune to the virulent tubercle bacilli; also that he by the same process could overcome tuberculosis already established.

There are also two facts that cannot fail to strike the observer. The first is, that a period of over seven years had elapsed from the date of his first publication on the tubercle bacillus and that announcing his discovery of the toxic agent; and the second, that his researches after the substance must have commenced about the period of Dr. Dixon's publication of October, 1889, of which, however, no mention is made in his address. It does not seem unfair to infer that Professor Koch had been unsuccessful during the preceding years in arriving at any satisfactory results. His own words, "My researches on this substance, therefore, although they have occupied me for nearly a year," etc., seems conclusive on this point. We do not, however, propose to do more than call attention to the coincidence of his researches after the toxic agent and the publication of Dr. Dixon's, October, 1889, the importance of which would be obvious to any bacteriologist, and the unfruitful nature of the former's investigations previous to that date.

There was, perhaps, a feeling prevalent in the medical world of incompleteness in the terms of Professor Koch's announcement, and it seems as if he had only stimulated curiosity in order to deny it satisfaction. Nor was this allayed when the news arrived from Berlin that the scientist, having brought his researches to a point sufficiently advanced to justify the use of his remedy in

corpore vili, was prepared to inoculate the human subject. But the nature of his remedy and the method of its composition were to be kept a profound secret.

The first inoculation into the human economy took place on September 22d, in a case of lupus, but it was not until the first week in November that it was given out that Professor Koch was ready to make inoculations on a general scale. It is not germane, however, to our purpose to do more than refer in passing to these events, or the exodus to Berlin, which is fresh in the public mind.

On November 15th Dr. Dixon, in the *Philadelphia Times and Register* (medical), clearly explained his position, as well as the result of his experiments up to that date. He wrote: "The hypothesis advanced in my terse article in the *Medical News* of October, 1889, have given the most brilliant results; yet I have never felt that the time had arrived for me to experiment on the human subject. Nor do I mean to be tempted to take any risks until the act would be purely an unselfish one. Even with the results that have been obtained in my laboratory, I would be sorry to have the general public stimulated with the idea that inoculation for tubercular phthisis had been perfected.

"Owing to the rumored report that Professor Koch has been, and is, inoculating human beings, it behooves me to await his results and understand his methods. If, however, it should appear that he is working on different lines, and that his plan is less dangerous than my own, it will be welcomed and adopted by me."

On November 18th Dr. Dixon laid before the Academy of Natural Sciences a report summarizing in more detail his work of investigation on the tubercle bacillus. After alluding to the capability of the bacillus of changing from its commonly recognized rod-form to that of a more compound one, club-shaped, curved, or branched, which he believed to be either involution or degenerate forms, he went on to say: "There would appear to be in this homogeneous mass something other than the bodies of the micro-organisms. This may be the residue of the pabulum remaining after the bacilli have selected what was necessary for their existence, or a digestive secretion, or again it may be an

excretion of the live organism. Let this be as it may, I hoped to find a changed functional action in the organism, in secretion or its excretion, that would combat tuberculosis in animal life, either by stimulating the cells or by causing a chemical reaction in the tissues that were susceptible to the digestive secretion of the tubercle bacillus.

An attempt to explain its probable action appears in an article I wrote for the *Medical News* of October 19th, 1889, and also in the *Medical and Surgical Reporter* and the *Times and Register* of this year. The views expressed are, however, purely hypothetical.

When the mass that I have already spoken of as being found on the pabulum was subjected for a considerable length of time to various degrees of heat, and injected into the guinea-pig, the animal seemed to sicken, yet only for a short time. The animals so treated appear to resist injections of virulent bacilli. Whether this would produce immunity for any length of time, provided we discontinue the administration of the remedy, I am not sure. Some animals injected with the virulent matter after the treatment with the changed mass had been discontinued appear to be immune, and experiments on animals suffering with tuberculosis have resulted most satisfactorily.

It is evident from this report that Dr. Dixon had pushed his ideas advanced on October 19th, 1889, to a stage promising to confirm in a remarkable degree the hypotheses laid down in his monograph, and that inoculation by the toxic agent had yielded most satisfactory results.

It cannot fail also to be remarked that there is a definiteness of statement, as far as the circumstances will admit, in Dr. Dixon's announcements which are lacking in those of his German colleague.

It soon became evident to Professor Koch that the attempt to withhold the composition of his remedy after it had been supplied to the profession was likely to defeat its own object. He therefore published on January 15th, 1891, a statement disclosing the nature of the remedy.

In this communication, after speaking of the preventive and curative effects of inoculating by living tubercle bacilli, he says:

"This effect is not exclusively produced with living tubercular bacilli, but is also observed with the dead bacilli, the result being the same whether, as I discovered by experiments at the outset, the bacilli are killed by a somewhat prolonged application of a low temperature or boiling heat, or by means of certain chemicals. This peculiar fact I followed up in all directions, and this further result was obtained—that killed pure cultivations of tubercular bacilli, after rinsing in water, might be injected in great quantities under healthy guinea-pigs' skin without anything occurring beyond local suppuration. If the injections are continued at intervals of from one to two days, the ulcerating inoculation wound becomes smaller and finally scars over, which otherwise it never does; the size of the swollen lymphatic glands is reduced, the body becomes better nourished, and the morbid process ceases, unless it has gone too far, in which case the animal perishes from exhaustion. By this means the basis of a curative process against tuberculosis was established."

We have italicized these words in order to call the reader's attention in connection with their identical nature with the following statement by Dr. Dixon, published months before: "That by submitting a mass of growing bacilli to different degrees of heat, etc., and injecting the mass into animals, he not only prevented tuberculosis, but also cured the same."

Compare this with Koch's just-published claim, that by injecting tubercle bacilli that had been submitted to solar light, heat, etc., he had produced in guinea-pigs immunity, and also cure, and moreover that by this the curative process against tuberculosis was established, and if there is any difference between the two, we have not been able to detect it.

With this last utterance of Prof. Koch the literature on the subject of the cure for tuberculosis for the present ceases.

We have endeavored to lay before our readers a succinct and chronological account of the history of this great discovery.

The important question as to whom belongs the credit for it, and to whom should be awarded the priority, may well be left to them. We venture to think that the material is present here before them to enable them to form a correct judgment.

